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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,799	12/05/2003	Itai Adin	225548	2262

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EXAMINER

QAZI, SABIHA NAIM

ART UNIT PAPER NUMBER

1616

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/729,799

Applicant(s)

ADIN ET AL.

Examiner

Sabiha Qazi

Art Unit

1616

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1616

Non Final Office Action

Claims 1-27 are pending. No claim is allowed. A terminal disclaimer has been filed and approved for co-pending application 10/341,690

Presently claimed invention is drawn to trihalogenated halobetasol propionate, which is marketed in US as Ultravate cream and Ultravate ointment as anti-inflammatory agent. The reference KALVODA et al. US Patent 4,619,921 discloses this compound in crystalline form having m.p. 220-221 C (example 5).

1. Claims 25-27 are rejected under 35 U.S.C. 102(b) as being anticipated by KALVODA et al. (US Patent 4,619,921). See (1) in col. 1, compound (II) in col. 2, lines 38-41 in col. 6 and example 5. The resulting compositions are expected to be the same as disclosed by the reference.

In an event where the composition as claimed may have different use, the two different intended uses are not distinguishable in terms of the composition, see *In re Thuau*, 57 USPQ 324; *Ex parte Douros*, 163 USPQ 667; and *In re Craige*, 89 USPQ 393.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1616

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over United States Patent No. 4,619,921, Brittain, H.G., (polymorphism in pharmaceutical solid, *Drugs and the pharmaceutical sciences*, vol. 95, 1999, chapter 6, pages 227-240; reference 1) and Brittain, H.G., (polymorphism in pharmaceutical solid, *Drugs and the pharmaceutical sciences*, vol. 95, 1999, chapter 6, pages 348-361; reference 2). See the entire documents.

Presently claimed invention is drawn to trihalogenated halobetasol propionate, which is marketed in US as Ultravate cream and Ultravate ointment as anti-inflammatory agent. The reference KALVODA et al. US Patent 4,619,921 discloses this compound in crystalline form

Art Unit: 1616

having m.p. 220-221 C. Example 5 discloses crystalline halobetasol propionate. The compound was re-crystallized methylene chloride/ether.

Brittain teaches (ref. 1) that compounds may be polymorphs i.e. forms having the same chemical composition but different crystal structures (introduction on page 228). See also fig. 1 on page 233. Different X-ray powder diffraction pattern is observed for each suspected polymorphic variation. See also X-ray Powder diffraction on page 235 where the technique of X-powder diffraction is disclosed as predominant tool for the study of polycrystalline materials and is eminently suited for routine characterization of polymorphs and solvates. The X-ray diffraction will therefore consist of a series of peaks detected as characteristic scattering angles. See page 236, first paragraph.

Brittain also teaches (ref. 2) changes in crystal forms affected by compaction and exemplified by applying to various useful drugs. See the entire document. See also fig. 7 on page 349 and figure 8 on page 352.

It would have been obvious to one skilled in the art to prepare various polymorphs of the known drug halobatasol because process of making polymorphs are known by various methods as cited in Brittain references. Different polymorphs are expected for a given compound, which would result in different X-ray powder diffraction pattern. One would have been motivated to prepare instantly claimed invention since it has long been the practice in the chemical and pharmaceutical arts to produce compounds in the form of crystals in pure form and may have different polymorphic forms. Changing the physical form, purity, enhanced deliverability etc of

Art Unit: 1616

an old product does not render the compound or the composition patentable because the difference in physical forms, purity etc was inherent in or rendered obvious by the prior art. See *In re Cofer*, 148 U.S.P.Q. 268 (CCPA) 1966). Some polymorphic forms may be more stable than the other depending on arrangements of atoms. One of the skilled in the art would have been motivated to prepare different crystalline e forms of known pharmaceutically useful compounds with the expectation of obtaining useful benefits such as longer shelf life, stability, enhanced deliverability, etc.

In absence of a showing of a viable unexpected property not only the X-ray diffraction pattern or stability, which are obvious to one skilled in the art, presently claimed invention of various forms of polymorphs and composition of a known compound halobetasol propionate and its X-diffractions would have been *prima facie* obvious to one skilled in the art. Furthermore, that one skilled in the art would know process of purification by crystallization of a compound because crystallization is a empirical skill well taught and recognized in the chemical art as is clear from the teachings by Brittain references cited above.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day.

Art Unit: 1616

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Padmanabhan, Sreeni (acting) can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Friday, December 09, 2005



SABIHA QAZI, PH.D
PRIMARY EXAMINER